L Number	Hits	Search Text	DB	Time stamp
1	1807	tyrosine adj phosphatase	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2003/08/27 17:55
2	407772	inhibit	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2003/08/27 18:31
3	236	(tyrosine adj phosphatase) with inhibit	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2003/08/27 17:56
4	211261	liver or fat	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2003/08/27 17:57
5	6	((tyrosine adj phosphatase) with inhibit) same (liver or fat)	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2003/08/27 18:04
6	7417	rondinone.in. or trevillyan.in. or zinker.in. or waring.in. or jirousek.in. or butler.in. or cowsert.in. or monia.in. or wyatt.in.	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2003/08/27 18:05
7	14	(tyrosine adj phosphatase) and (rondinone.in. or trevillyan.in. or zinker.in. or waring.in. or jirousek.in. or butler.in. or cowsert.in. or monia.in. or wyatt.in.)	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2003/08/27 18:17
8	12	(liver or fat) and ((tyrosine adj phosphatase) and (rondinone.in. or trevillyan.in. or zinker.in. or waring.in. or jirousek.in. or butler.in. or cowsert.in. or monia.in. or wyatt.in.))	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2003/08/27 18:28
9	1702	phosphotidylinositol	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2003/08/27 18:28
10	2	((liver or fat) and ((tyrosine adj phosphatase) and (rondinone.in. or trevillyan.in. or zinker.in. or waring.in. or jirousek.in. or butler.in. or cowsert.in. or monia.in. or wyatt.in.))) and phosphotidylinositol	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2003/08/27 18:30
11	2	(((tyrosine adj phosphatase) with inhibit) same (liver or fat)) and phosphotidylinositol	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2003/08/27 18:30
12	51	(tyrosine adj phosphatase) and inhibit and phosphotidylinositol	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2003/08/27 18:33
13	50	(tyrosine adj phosphatase) and inhibit and phosphotidylinositol and (liver or fat)	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2003/08/27 18:42

14	1	(detect$ with phosphotidylinositol) same (liver or fat)	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2003/08/27 18:43
15	2	(detect$ with phosphotidylinositol) and (liver or fat)	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2003/08/27 18:44

US-PAT-NO: 5593678

DOCUMENT-IDENTIFIER: US 5593678 A

TITLE: Protection of teleost fish

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Detailed Description Text - DETX (57):
The notion that phosphatases might be involved in the process of regulation of NCC cytotoxicity is compatible with several other observations. For example, phosphatase inhibitors (e.g., LiCl) was required in experiments to detect increased levels of phosphotidylinositol metabolites (i.e., PIP.sub.3) which appear during cell triggering responses. Lithium chloride specifically inhibited phosphotidylinositol phosphate phosphatase activity. Other phosphatase inhibitors (zinc chloride, sodium fluoride, okadaic acid, etc.) have been used in numerous studies to demonstrate the build-up of phosphoproteins following agonist binding. Also, mab 5C6 binding to an NCC receptor molecule activated cytotoxicity Evans et al. (1990) supra, initiated the release of free cytoplasmic calcium [Evans et al. (1990) Dev. Comp. Immunol. 14:295; Evans et al. (1992) supra] and caused increased levels of IP3 production. Increasing and prolonging levels of protein phosphorylation could thus be associated with increased cytotoxicity.

Detailed Description Text - DETX (58):
The present studies which show that alterations in dephosphorylation by phosphatase inhibitors affect cytotoxicity are supported by studies demonstrating that vanadate stimulated cellular

carbohydrate biosynthetic
pathways. Vanadate has insulin-mimetic activity as demonstrated by studies
showing: augmentation of insulin binding [Fantus et al. (1990) Endocrin.
127:2716], prolongation of insulin activity [Fantus et al. (1990) supra],
stimulation of glucose oxidation [Schechter et al. (1980) supra], and
stimulation of glycogen synthetase activity [Tamura et al. (1984) Supra].
Vanadate directly activated kinases in rats [Gill et al. (1988) supra], in
transformed human B-cells [Earp et al. (1983) supra] and rat adipocytes
[Ledbetter et al. (1988) supra]. Oral administration of vanadate to rats (15
.mu.M in the drinking water) caused normalization of blood glucose levels in
diabetic animals. In rats, vanadate also stimulated glucose transport into
muscles and liver and improved cardiac performance. These effects were
reversible within two days following termination of feeding [Meyerovitch et al.
(1987) supra]. In these studies, there was no evidence that vanadate produced
any irreversible changes in these treated rats.

Detailed Description Text - DETX (147):
a. The levels of NCC in various lymphoreticular tissue as a variable of
vanadate treatment are determined. Single cell suspensions are prepared from
the following fish tissue: PBL, spleen, thymus, liver, anterior kidney and
trunk kidney. Absolute numbers of NCC will be determined by flow cytometric
analysis with mab 5C6.

Detailed Description Text - DETX (150):
d. Histological changes in lymphoreticular tissue are measured following
vanadate treatment. At each sampling time for cytotoxicity determination,
e.g., flow cytometry, etc., tissue will be taken for

histological evaluation.
These tissue will consist of anterior kidney, brain, spleen, liver, trunk
kidney and thymus.